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LOUIS MYERS
FISH & RICHARDSON PC
225 FRANKLIN STREET
BOSTON MA 02110-2804

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EXAMINER

GABEL, G

ART UNIT

PAPER NUMBER

1641

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/394,265

Applicant(s)

WOLF, DAVID E.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 18-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-24 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 14) ☒ Notice of References Cited (PTO-892)
- 15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 17) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 18) ☐ Notice of Informal Patent Application (PTO-152)
- 19) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-17, drawn to method of evaluating carbohydrates in vitro, classified in class 436, subclass 501, for example.
 - II. Claims 18-22, drawn to method of using sensor to evaluate carbohydrate level in vivo, classified in class 436, subclass 172, for example.
 - III. Claims 23-24, drawn to a sensor, classified in class 424, subclass 9.6, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation and function such as the method of Group II measures human carbohydrate levels using a sensor modified to function in vivo under physiological conditions and the method of Group I measure human carbohydrate levels using a sensor specifically adapted for in vitro laboratory testing.

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Inventions I and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, carbohydrate levels can be determined by measuring oxidation of carbohydrates such as glucose using polarographic glucose sensor.

Inventions II and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, carbohydrate levels can be measured in vivo by subcutaneously introducing glucose oxidase into the skin then detecting enzymatic reaction.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because the search required for Group I is not required for Group II, and the search for Group II is not required for Group III, restriction for examination purposes as indicated is proper. Literature search for each method and apparatus is distinct since the structural requirements of each invention are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

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During a telephone conversation with Dorothy Whelan on 10/24/00 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-17. Affirmation of this election must be made by applicant in replying to this Office action. Claims 18-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Accordingly, claims 1-17 are under examination for prosecution on the merits.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached). Correction is required. However, formal correction of noted defect can be deferred until application is allowed by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "reduced" in claim 1 is a relative term which renders the claim indefinite. The term "reduced" is not defined by the claim, the specification does not

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provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also claims 2, 3, 7, 15, and 17.

Claim 4 is vague and indefinite in reciting "important in dimer-dimer interactions to produce dimers which do not assemble into tetramers " because the term "important" is a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 6 is vague, indefinite, and incomplete in reciting "Concanavalin A contains a mutation at one or more ... amino acid positions" because site specific mutagenesis of the protein at specific amino acid positions is recited in the absence of a base (reference) sequence, thereby, omitting an essential element in the claim.

Regarding claim 8, the phrase "or a portion thereof" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "or a portion thereof"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

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patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-17 are rejected under the judicially created doctrine of double patenting over claims 1-17 of the Wolf patented application, ASN 09/090,601 (under process for allowance, belonging to David E. Wolf) since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant invention is fully disclosed in the patented application of the Applicant (Wolf patent: ASN 09/090,601) and is covered by the Wolf patent since the Wolf patent and the instant application are claiming common subject matter, as follows: method of evaluating carbohydrate in a sample using specifically reduced valency carbohydrate binding ligands (CBL) wherein the recombinant reduced valency CBL in the instant application is structurally equivalent to the low valency CBL having no greater than three carbohydrate binding sites claimed by the Wolf patent because both CBL structures are essentially and necessarily non-tetrameric with reduced valency. With the knowledge taught in the Wolf patent, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to map epitopic specificities of recombinant CBL so as to identify epitopes that are specific to carbohydrate or glucose and therefrom, mutate or splice the selected corresponding amino acid positions to obtain a desired reduction in valency of these CBLs such as taught in the Wolf patent because epitope mapping, manipulation of valency levels in

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binding ligands, and site specific selection of epitopes for mutagenesis in certain amino acid positions for the purpose of exclusion in binding reactivities is well known and conventional in the art. Further, the recombinant reduced valency CBL in the instant application constitutes an obvious variation in species of the low valency CBL taught in the Wolf patent.

Furthermore, there is no apparent reason why Applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3-4, 7-17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chick et al. (US 5,342,789).

Chick et al., from here on Chick, discloses a method for identifying and quantifying concentration of carbohydrate analytes, i.e. glucose and mannose, in blood, body fluids, and other samples such as cellular homogenates using non-radiative fluorescence resonance energy transfer or FRET (see Abstract, column 4, lines 47-54,

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and Example 3). Chick specifically discloses contacting two fluorescently-labeled binding partners or energy absorbing FRET components with a blood or body fluid sample. A variety of modes of placing the specific binding pairs (reactants) in communication with glucose (in vivo embodiment) are employed such as encapsulation in an immunoisolating capsule or microcapsule (microdialysis vessel or in spheres) (see column 9, lines 1-23). Chick uses FRET to determine the occurrence and extent of binding between the specific binding pairs, which is competitively decreased by a carbohydrate (see column 4, lines 22-44). The first binding pair is a low valency CBL such as lectin or concanavalin A (Con A) and the second binding pair is a glycoconjugate with a carbohydrate moiety such as glycosylated (bovine) albumin which specifically binds to the ligand in competition with carbohydrate or glucose. Competition with the carbohydrate occurs in a dose dependent manner and reversible (see column 2, lines 17-33, column 6, lines 43-54, Figure 2, and column 12, lines 14-19). Each member of these energy absorbing components is labeled with a different fluorophore (see column 4, lines 55-65). Chick discloses that in FRET, the ligand can be labeled with a donor molecule and the glycoconjugate can be labeled with an acceptor or vice versa wherein FRET occurs only when donor and acceptor molecules are sufficiently close in proximity (generally within 100 angstroms) to one another. The excited state energy level of the first light absorbing FRET component overlaps with the excited state energy level of the second light absorbing FRET component (see column 2, lines 47-54 and Figure 1). When these two light absorbing materials with overlapping excited state

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energy levels are in sufficiently close proximity with each other, a resonance dipole-induced dipole interaction occurs which results to the transfer of excited state energy of the donor molecule to the acceptor molecule and further results in quenching of the donor fluorescence and sensitized emission of the acceptor. FRET results when CBL and glycoconjugate in the sample bind except in the presence of carbohydrate wherein the ligand and the glycoconjugate are competed off. The presence and concentration of carbohydrate in the blood sample is indicated as a decrease in the efficiency of energy transfer measured by a fluorimeter (see column 2, lines 33-47 and column 3, lines 13-18). Figure 4 shows that the FRET method is able to predict glucose concentrations accurately using a reliable sensor for detecting glucose concentrations (calibrated to detect) over the entire physiologic range (see also column 8, lines 6-40 and column 11, lines 17-23).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2 and 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chick et al. (US 5,342,789) in view of Cho et al. (Trends in Glycoscience and Glycotechnology, January 1997, Abstract).

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Chick has been discussed supra. Chick fails to disclose the reduced valency CBL (lectin) as recombinant monomeric form of lectin and wherein the lectin is mutagenized at specific residues to produce dimers that do not assemble into tetramers.

Cho et al., from here on, Cho teaches the mechanism of dimerization of lectin (galectin-1) to study the functional differences between the monomeric and dimeric forms by specifically mutating the extreme N-terminal region that is involved in binding interactions. Cho teaches that the dimeric forms of recombinant (mutated) lectin can be covalently cross-linked to create extremely potent binding activity (agglutinin) and the monomeric forms compete with the dimers to block their binding.

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in synthesizing recombinant forms of reduced valency CBL or recombinant monomeric/dimeric lectin such as taught by Cho for use in the method for evaluating carbohydrate levels such as disclosed by Chick because production of recombinant polypeptides, epitope mapping, manipulation of valency levels in binding ligands, and site directed mutagenesis in certain amino acid positions for the purpose of exclusion in binding reactivities is well known and conventional in the art and Cho specifically compared monomeric and dimeric binding characteristics of recombinant lectin mutations in the N-terminus which is involved in binding interactions and Chick specifically disclosed evaluating carbohydrate level in a sample by binding lectin with a glycoconjugate that includes carbohydrate. One of ordinary skill in the art

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at the time of the instant invention would have been motivated to incorporate the teaching of Cho into the method of Chick because Chick specifically disclosed the need of a reliable and accurate method to detect a wide range of carbohydrate concentrations and by incorporating the teaching of Cho in recombinant lectin binding interactions and differentiation between their individual valencies with the method of Chick, an ordinary artisan may very well achieve an even greater extent of accuracy and reliability such as taught in the instant invention.

7. For reason aforementioned, no claims are allowed.

Remarks

8. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Lakowicz et al. (Analytica Chimica Acta, 1993) teach fluorescence assay of glucose based on Fret and phase-modulation measurements.

Mandal et al. (Biochemistry, 1993) teach that dimeric Con A and native tetrameric Con A have differences in binding affinities with large oligomannose-type glycopeptides.

Stubbs et al. (Journal of Biological Chemistry, 1986 (Abstract)) teach an experimental system in which specific amino acid alterations can be introduced into the carbohydrate binding ligand site of pea lectin and found that there is no detectable

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difference in the carbohydrate binding properties between native and recombinant lectin.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gail Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

G. Gabel 11/27/00

Gail Gabel
Patent Examiner
Group 1641

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800-1641